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SECTION OF BIOLOGY[1]

JANUARY 8, 1940

DOCTOR H. JENSEN, The Squibb Institute for Medical Research, New Brunswick, N. J.: *Our Present Knowledge of Carbohydrate Metabolism.* (This lecture was illustrated by lantern slides.)[2]

Normal carbohydrate metabolism is dependent upon the proper physiological coordination of various biologically active agents. The different phases of carbohydrate metabolism are intimately linked with that of proteins and fats. Apparently one cannot have abnormal protein or fat metabolism without a disturbance in the utilization of carbohydrates.

It is perhaps advisable to present only a brief description of the main phases of carbohydrate metabolism observed in normal animals. Dextrose (d-glucose) is the sugar which is most efficiently metabolized by the tissues of the organism and other sugars are generally converted into glucose by the liver before they can be utilized. It is well established that

[1] No meetings were held in January by the Sections of Geology and Anthropology.

[2] This lecture was announced under the title "Our Present Knowledge of Diabetes Mellitus."

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certain amino acids present in proteins can be converted into carbohydrate by the liver. The possibility of the conversion of fat into carbohydrate, however, has not yet been definitely proven.

Absorbed sugar is either oxidized in the tissues or converted into glycogen in the liver and muscle. Little is known of the various intermediary products of the oxidation of glucose to carbon dioxide and water or of the synthesis and breakdown of liver glycogen. It is evidently a rapid and constantly occurring process. Glucose is burned for energy in the various tissues of the body. Muscle glycogen is oxidized to lactic acid, thus furnishing the energy for muscular activity. Part of the lactic acid is then transformed into glycogen in the liver.

The concentration of glucose in the blood is of importance in supplying the various cells with sugar. The maintenance of a fairly constant blood sugar level depends on the proper balance between the mechanism for disposing of sugar in the blood and that responsible for replenishing it. Glycogen formation in the liver and muscles and in other tissues, together with oxidation and excretion of glucose, disposes of the blood sugar. On the other hand, the liberation of glucose from liver glycogen and the absorption of carbohydrate from ingested food may replenish the decreased amount of sugar in the blood. The efficiency with which these regulatory mechanisms counteract each other depends to a large extent on a normal endocrine balance. Any relative or absolute deficiency or preponderance of certain endocrine secretions may result in either an increase (hyperglycemia) or a decrease (hypoglycemia) of the sugar in the blood.

In the following presentation I shall attempt to discuss briefly our present knowledge of the influence of certain hormones on the metabolism of food stuffs. The exact rôle which each of the different endocrine principles plays in the process of metabolism[3] has not yet definitely been established.

[3] When I speak of metabolism I refer to that of fat, protein and carbohydrate.

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Insulin: Insulin, the internal secretion of the pancreas, is formed in the islet tissue of that organ and passes from there into the general circulation. Its presence is indispensable for the normal maintenance of metabolism in mammals. The importance of insulin with regard to metabolism becomes evident upon examination of the physiological disturbances in the body which one observes in the absence of the secretion of insulin (pancreatectomy, diabetes mellitus). The following symptoms have been found to be characteristic:

(1) Pronounced hyperglycemia and glycosuria.

(2) Depletion of the glycogen stores in certain tissues (liver, muscle).

(3) Lowering of the respiratory quotient indicating incomplete combustion of glucose.

(4) Increase in the glucose-nitrogen ratio in the urine probably due to an increase in the conversion of protein into glucose.

(5) Development of acidosis probably caused by imperfect fat metabolism.

Injection of insulin will relieve all these symptoms and reestablish a practically normal metabolism. Administration of insulin also effects specifically the carbohydrate metabolism of the normal organism.

The following functions may be attributed to insulin:

(1) Acceleration of glucose oxidation in the tissues.

(2) Increase in the rate at which glucose is converted to glycogen in the muscle and in other tissues. It is still unsettled whether insulin has a direct influence on the formation of liver glycogen or whether it inhibits hepatic glycogenolysis which is caused by certain other hormones. This inhibitory effect of insulin would enable the liver of the normal animal to retain its glycogen, and would also account for the disappearance of liver glycogen in the depancreatized animal (absence of insulin).

Increase in glucose oxidation and in the rate of glycogen formation probably accounts for the fall in blood sugar observed after insulin injection.

(3) Inhibition of carbohydrate formation in the liver from non-carbohydrate sources. Gluconeogenesis is apparently under the control of certain other endocrine principles.

(4) Prevention of the formation of ketone bodies which are formed as a result of incomplete carbohydrate metabolism.

Decrease in glucose oxidation and increase in hepatic glycogenolysis and gluconeogenesis suggests that hyperglycemia may be due to the following factors:

(a) Deficient supply of insulin.

(b) Liberation, either at a normal or excessive rate, of those principles which play a rôle in glycogenolysis and in gluconeogenesis.

Anterior Pituitary: Knowledge of the complex relationship of the secretion of the anterior pituitary to carbohydrate, protein and fat metabolism is at present still incomplete. It is as yet not known whether any of the anterior pituitary principles exert a direct effect on certain phases of the metabolism of food stuffs or whether this influence is solely mediated through certain other endocrine organs such as the adrenals and thyroids.

That the anterior pituitary is associated in some way with carbohydrate metabolism is shown by the following observations:

(a) Removal of the pituitary gland renders the animal more sensitive to insulin. As compared with normal animals, the glycogen stores of the liver and muscles are more rapidly depleted on fasting. Injection of anterior pituitary extracts will prevent this depletion of the glycogen stores and will render the animal more resistant to insulin.

(b) The symptoms of experimental diabetes (removal of the pancreas) are greatly ameliorated following hypophysectomy. The diabetic symptoms are manifested again upon injection of anterior pituitary extracts into such doubly operated animals.

(c) Recently it has been found that a diabetes-like effect can be produced in normal dogs by the daily injection of in-

creasing amounts of anterior pituitary extracts over a period of several days or weeks. The same effect can be obtained more readily in partially depancreatized animals.

Adrenal Cortex: In general it may be said that the influence of this endocrine organ is similar to that of the anterior pituitary. It is known that the functional integrity of the adrenal cortex is under the control of the anterior pituitary. The effect of the secretion of the adrenal cortex on metabolism is indicated by the following experimental findings:

(a) Adrenalectomized animals show a marked decrease in liver glycogen, particularly on fasting, a lowering in muscle glycogen and blood sugar and an increased sensitivity to insulin. Injection of cortical extracts restores the depleted carbohydrate stores and renders the animal more resistant to insulin.

(b) Removal of the adrenal cortex greatly ameliorates the diabetic symptoms observed in totally depancreatized animals. Administration of cortical extracts causes the reappearance of glycosuria in the adrenalectomized-depancreatized animal.

(c) Injection of cortical extracts into partially depancreatized animals produces an increase in blood sugar and glycosuria. In normal animals, a marked increase in liver glycogen, a slight elevation of the blood sugar level and an increase in nitrogen excretion can be observed.

(d) Depletion of liver glycogen of the fasted hypophysectomized animal can be prevented by the administration of cortical extracts.

(e) An anti-insulin effect can be produced by the injection of either adrenotropic pituitary fractions or of cortical extracts (corticosterone).

The effects of the adrenal cortex on metabolism are strikingly similar to those produced by the anterior pituitary. This has a direct bearing on the question of the participation of the adrenal cortex in the metabolic activity of the anterior pituitary.

The observations on the influence of the anterior pituitary

and the adrenal cortex on metabolism suggest that overfunction of these endocrine organs might sometimes give rise to the symptoms of diabetes mellitus.

Thyroid: It has been known for a long time that the secretion of the thyroid has a decided effect on metabolism. The exact rôle which the secretion of this gland plays on the various phases of metabolism, however, is little understood at the present time.

Conclusions: I have attempted to show that carbohydrate metabolism is the resultant of a well-balanced interaction of various endocrine principles. The changes in metabolism are controlled, on the one hand, by insulin and, on the other hand, by those endocrine secretions (anterior pituitary, adrenal cortex and thyroid) which are apparently antagonistic to the physiological action of the pancreatic hormone. The exact manner in which these endocrine principles divert metabolism in one direction or another is still unknown. Perhaps, one may consider them as mediators in some enzymatic processes concerned with metabolism. The view that normal metabolism is dependent on the physiological coordination of various active agents in the body would seem to offer a reasonable and harmonious interpretation of the various experimental findings on metabolism.

SECTION OF PSYCHOLOGY

JANUARY 15, 1940

PROFESSOR C. J. WARDEN, Columbia University: *The Ability of Monkeys to Use Tools.* (This lecture was illustrated by motion pictures.)

The lecture covers very briefly various aspects of a project which has been in progress since 1935 on this general topic, supported by the Council for Research in the Social Sciences of Columbia University, under the direction of the speaker.

It has been the general impression until fairly recently, that the use of tools (manual instrumentation) is limited to man's closest Primate relatives, the Great Apes (Orang-utans, Gibbons, Chimpanzees, Gorillas). The assumption was that this capacity evolved in a rudimentary form at this level and was passed on to become highly elaborated in man as he evolved toward his present level. More recently, however, a number of workers have reported that monkeys—the next lower Primate level—possess some tool-using ability, as shown by the use of a single string, stick, or rake in securing food placed out of reach. The aim of the present project was to explore this type of ability in Old World monkeys (*Rhesus*) and New World monkeys (*Cebus*) and determine the limits of complexity which such types might reach by training, and also to compare the ability of the two major lines of monkey evolution. The animals were tested in a work cage of suitable size, with bars through which rakes (T-sticks) could be manipulated on a platform outside, on which a food-cup containing one-fourth of a peanut could be placed out of reach.

The first task was to develop the ability to use a single rake effectively and regularly in securing the food, when the rake was placed just in front of the bars with no clear connection with the food-cup beyond. The *Cebus* monkeys were more adept at this than the *Rhesus* monkeys from the start, and became efficient in about half the number of trials re-

quired by the *Rhesus* type. After the use of a single rake had been well mastered, the task was to use a short rake to drag in a longer one, the latter being long enough to reach the food-cup. After this stage was learned, 3 rakes were employed, then 4 rakes, and so on up to an 8-rake set-up. In time, all of the 6 monkeys (3 *Cebus,* 3 *Rhesus*) reached the stage at which 4 rakes were required. Even the 8-rake series was mastered by 2 *Cebus* and 1 *Rhesus* monkey. The tests were stopped at this point because the last rake of the series was now so long that the animals had trouble using it effectively. In fact, it was about twice the length of their bodies and was also quite heavy. It seemed clear to the experimenters that some of the brighter monkeys had generalized the task, in some sense, so that a much longer series of rakes might have been manipulated successfully, except for the hard labor involved.

Some two years later, it was decided to complicate the task by placing the rakes on 2 and 3 platforms, each located on a different side of the cage. This arrangement forced the monkeys to bring rakes from one platform into the cage, turn them with the cross-bar end out, and push them through the bars to the other platforms. They also had to judge the lengths of the rakes so as to use them in the correct order. Moreover, the rakes were placed in a mixed order, as regards length, so as to get away from the routine serial factor in the experiment described above.

Although it had been two years since the monkeys had worked on the single platform task, this was readily reinstated after a few trials in the *Cebus* monkeys. The *Rhesus* type required 300 to 400 trials here. Thus again the *Cebus* show a marked superiority to the *Rhesus*—this time in the *retention* of the habit after the lapse of two years. Both of the *Cebus* monkeys mastered the 8-rake series of the 2-platform set-up, and apparently might have gone much further with more training. One *Rhesus* mastered the 7-rake series here but the other one could not go beyond the 4-rake series.

The best *Rhesus* and the 2 *Cebus* monkeys were then tested on the 3-platform set-up with the following results:—the *Rhesus* failed beyond the 7-rake series; one *Cebus* learned the 11-rake series, and the other, after passing the 8-rake test, was discontinued because of a hand injury. It was felt that these records represent about the limits of ability of the two types of monkeys. The point should be stressed, however, that the use of 7 to 11 rakes in a mixed order on 3 platforms means a fairly well developed ability in intelligent manual instrumentation. We conclude, therefore, that this capacity evolved at least as early as the monkey level in the Primate line, and not at the great ape level as has hitherto been supposed.

It was then decided to see to what extent such habits would be retained following extirpation of one or both frontal lobes (pre-motor area forward). The operations were done by Dr. S. E. Barera of the New York State Psychiatric Institute, and the post-operational tests were made by Dr. Wm. Galt of the Lifwyn Foundation at the Columbia University animal laboratory. This work has just been completed and a full report of the findings cannot be made until the results have been properly analyzed. However, I can make a few general statements as to the main facts, but prefer to offer no interpretations at present. Unilateral extirpation did not appear to disturb the habit of using rakes in series on a single platform. The simpler levels of the 2- and 3-platform habits (up to 3-rake series) were still retained, while the more complex habits were not. Perhaps, continued re-training (post-operational) might have brought about the re-instatement of the latter, in part or in whole. Bilateral extirpation still left the single-platform habit intact or, at most, only slightly reduced at the higher levels. The multiple-platform habits, however, were seriously affected. On the 2-platform set-up, the animals failed beyond the 2-rake level and on the 3-platform set-up, they failed altogether.

The results of the project as a whole indicate the presence

of a simple but definite tool-using capacity in both Old and New World monkeys. Manual instrumentation habits, once learned, are retained with little loss over a period of two years or more—especially in the *Cebus* type. The *Cebus* seems to rate above the *Rhesus* in both learning and retention tests for the sort of task here employed. The simpler habit levels are not disturbed by unilateral and bilateral frontal lobe extirpation, whereas the more complex habits are not retained.

ANNOUNCEMENT OF PUBLICATIONS FOR 1940[1]

The following publications will be issued by the Academy during the current year. Members of the Academy who desire to receive these papers will kindly request the Executive Secretary to send them, and they will be mailed, free of charge, as they are ready for distribution, except as qualified in the footnotes:[2]

ANNALS:

1. "Kinetics in Solution." This article will contain the papers delivered at the conference of the Section of Physics and Chemistry, February 24 and 25, 1939. (About 100 pages.)
2. "Studies on the Nutrition of Colorless Euglenoid Flagellates," by Henry W. Schoenborn. (About 40 pages.)
3. "Studies in Chelonian Osteology; the Fossae and Temporal Arcades of Chelonian Skulls," by Herbert Ruckes. (About 35 pages.)
4. "Dielectrics." This article will contain the papers delivered at the conference of the Section of Physics and Chemistry, April 14 and 15, 1939. (About 100 pages.)
5. "The Distribution of Density Within the Stars," by Henry Norris Russell. (About 15 pages.)
6. "The Structure and Relationships of Protoceratops," by Barnum Brown and Erich M. Schlaikjer. (About 150 pages.)
7. "Free Radicals as Intermediate Steps in the Oxidation of Organic Compounds." This article will contain the papers delivered at the conference of the Section of Physics and Chemistry, November 10 and 11, 1939. (About 100 pages.)

[1] Notice of additional publications to be added to this list will be sent to members later.

[2] Student and Associate Members are entitled to receive one complete monograph or up to 150 pages.

TRANSACTIONS:

Series II, Vol. 2, Nos. 1–8. These papers are sent to all members of the Academy, regularly during the academic year. (About 150–200 pages.)

SCIENTIFIC SURVEY OF PORTO RICO AND THE VIRGIN ISLANDS:[3]

Volume XVIII, Part II: "Porto Rican Archeology," by Froelich G. Rainey. Published February 13, 1940.

Volume XII, Parts 2 and 3: "Insects of Porto Rico and the Virgin Islands—Heterocera," by William Schaus.

[3] The Scientific Survey publications are available to Members for $1.50 per part and to non-members for $2.00 per part.

A certain number of parts, as announced each year, are available free to Honorary, Life and Sustaining Members.